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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,321	10/26/2001	Liming Shao	SPV-045.01	1490

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	38

DATE MAILED: 08/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/041,321	Shao
Examiner	**Art Unit**
Gollamudi Kishore	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 2, 2002* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 7-10, 12-16, 18, 20, 21, and 23-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 7-10, 12-16, 18, 20, 21, and 23-29* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment dated 6-2-03 is acknowledged.

Claims included in the prosecution are 1-4, 7-10, 12-16,18, 20-21, and 23-29.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless -**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

2. Claims 1-4, 7-10, 12-16, 18, 20-21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 92/02256 of record.

WO discloses cyclodextrin complexes containing fentanyl, alfentanil, sufentanil and lofentanil for the treatment of pain (note the abstract, Examples and claim 16).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that WO does not give any examples of using fentanyl and this does not constitute the basis of rejection under 102 (b). The examiner disagrees. WO claims just 5 compounds in combination with cyclodextrin and provides an example for four of the compounds. One of the five claimed compounds in WO is fentanyl. Five is a reasonable number of compounds and hence the reference qualifies as 102 (b). Furthermore, if that were the rationale, then applicant's formula encompasses multitudes

of compounds and applicant himself has not provided examples for each of those compounds falling under said formula I.

3. Claims 1, 3, 7-10, 12-16,18, 20-21, and 23-26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Mezei (5,451,408) of record.

Mezei discloses liposomal formulations containing fentanyl for the treatment of pain (abstract, Examples and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant amends claim 1 to delete originally recited Markush member, 'liposomes' and argues that the rejection should be withdrawn. This argument is not found to be persuasive for the following reasons. Instant claim recites 'micelle forming agents' and not 'micelles'. Lecithin is known in the art as a micelle forming agent. The examiner cites the references of DE 3228629 (abstract), US 4,551,449 (col. 1, lines 23-27); US 4,320,121 (col. 10, lines 47-52) are cited of interest in this context. Instant claim language does not exclude the presence of liposomes.

4. Claims 1, 3-4, 7-10, 12-16,18, 20-21, and 23-26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/360071.

WO discloses fentanyl and fentanyl derivatives in polymeric carriers (note the examples and claims).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

6. Claims 1-4, 7-10, 12-16,18, 20-21, and 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/02256 cited above.

The teachings of WO 92/02256 have been discussed above. WO does not teach all of the claimed compounds falling under the basic structure of fentanyl and although WO teaches only handful compounds including fentanyl, it does not provide specific example using fentanyl. However, in the absence of showing the criticality, it is deemed obvious to one of ordinary skill in the art to encapsulate fentanyl or any compound based on the basic structure of fentanyl in the in the cyclodextrin compositions of WO with a reasonable expectation of success. WO also does not teach the method of treating pain in claimed animals. However, in the absence of showing otherwise, it is reasonable to expect that the compositions which are effective in rats would be effective in other animals and humans too.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant once again argues that WO does not provide examples and that the

molecules tested in WO are morphine and lofentanyl possessed significant differences in biological activity, thereby illustrating that relatively-modest changes in structural features of the constituent small molecule have a significant impact on the biological activity of the formulation in treatment of pain. This argument is not found to be persuasive since the inventive concept of WO is the use of cyclodextrins to enhance the effectiveness of the analgesics in pain management and Table 1 on page 15 of the reference shows that cyclodextrin enhanced the effectiveness of all the four drugs tested and therefore, one of ordinary skill in the art would reasonably expect the cyclodextrin encapsulation to enhance the analgesic activity of free fentanyl or related compounds. Furthermore, based on applicant's own argument (that is, 'relatively-modest changes in structural features of the constituent small molecule have a significant impact on the biological activity of the formulation in treatment of pain'), one would expect the same with numerous compounds formula I encompasses.

7. Claims 1-4, 7-10, 12-16,18, 20-21, and 23-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/36071 cited above.

The teachings of WO 99 have been discussed above. What is lacking in WO are the teachings of the administration of the compounds to species other than humans and the administration be oral. However, it is deemed obvious to one of ordinary skill in the art to administer the composition to any animal species with the expectation of obtaining similar results since in the art of biological and medical sciences, animals are used as models for

humans; mode of administration is deemed to be a manipulatable parameter and the choice of the practitioner of the art to obtain the best possible results.

The reference of Gale (4,588,580) which teaches fentanyl in combination with a polymer is cited of interest.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

August 4, 2003